PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Continuation Application of:	
KLAVENESS et al.	Office of Initial Patent Examination
Serial Number: 08/960,054	
Filed: This application filed: January 22, 2001	

For: IMPROVEMENTS IN OR RELATING TO DIAGNOSTIC/ THERAPEUTIC AGENTS

PRELIMINARY AMENDMENT

ASSISTANT COMMISSIONER FOR PATENTS
Washington, D.C. 20231

Sir:

Prior to an examination on the merits, please amend the above identified application as follows:

IN THE SPECIFICATION:

Please insert as the first sentence - -This application is a continuation application of pending U.S. application serial number 08/960,054, filed October 29, 1997, which has been allowed and the Issue Fee timely paid, which is a continuation-in-part of U.S. application serial number 08/958,993, filed October 28, 1997, which has been allowed and the Issue Fee timely paid.- -

IN THE CLAIMS:

Please cancel claims 1-37 without prejudice or disclaimer and add the following new claims to the application.

- -38. A targetable diagnostic and/or therapeutically active agent comprising a suspension of a reporter comprising gas-filled microbubbles stabilised by monolayers of film-forming surfactant in an aqueous carrier liquid, and

wherein the gas comprises a halogenated gas or a halogenated lower molecule weight hydrocarbon, and

said film-forming surfactant comprises a phospholipid, and

said agent comprising a lipid attached to a linker portion for covalent coupling to one or more vector molecules, and

where said vector(s) binding to receptors/targets at sites associated with angiogenesis, inflammation, atherosclerotic plaques and/or thrombi,

said linker portion optionally comprising a peptide linker portion.

39. An agent as claimed in claim 38 wherein the linker portion comprises two or more lysine molecules.

40. An agent as claimed in claim 38 wherein the halogenated gas comprises a perfluorinated ketone, perfluorinated ether, partially halogenated hydrocarbon or perfluorocarbon and/or mixtures thereof.

41. An agent as claimed in claim 38 wherein the halogenated gas comprises sulphur hexafluoride or a perfluoropropane, perfluorobutane or perfluoropentane.

42. An agent as claimed in claim 38 wherein the microbubbles bear a net overall charge.

43. An agent as claimed in claim 42 wherein the net overall charge is negative.

44. An agent as claimed in claim 38 wherein the film-forming surfactant material comprises one or more phospholipids selected from the group consisting of phosphatidylcholines, phosphatidylglycerols, phosphatidylinositols, phosphatidylserines, phosphatidyletanolamines and phosphatidic acid.

45. An agent as claimed in claim 38 wherein the film-forming surfactant material comprises a lipopeptide.

46. An agent as claimed in claim 38 which further contains moieties which are radioactive or are effective as X-ray contrast agents, light imaging probes or spin labels.

47. An agent as claimed in claim 38 further comprising a therapeutic compound.

48. An agent as claimed in claim 47 wherein said therapeutic compound is an antineoplastic agent, blood product, biological response modifier, antifungal agent, hormone or hormone analogue, vitamin, enzyme, antiallergic agent, tissue factor inhibitor, platelet inhibitor, coagulation protein target inhibitor, fibrin formation inhibitor, fibrinolysis promoter, antiangiogenic, circulatory drug, metabolic potentiator, antitubercular, antiviral, vasodilator, antibiotic, antiinflammatory, antiprotozoan, antirheumatic, narcotic, opiate, cardiac glycoside, neuromuscular blocker, sedative, local anaesthetic, general anaesthetic or genetic material.

49. An agent as claimed in claim 47 wherein said therapeutic compound is covalently coupled or linked to the reporter through disulphide groups.

50. An agent as claimed in claim 38 comprising a coupled polyethyleneglycol (PEG) element.

51. An agent as claimed in claim 50 comprising a polyethyleneglycol (PEG) element coupled directly to the reporter molecules.

52. An agent as claimed in claim 50 wherein a PEG element is used as a spacer between the vector and said lipid.

53. An agent as claimed in claim 38 wherein the vector molecule is an angiogenesis-specific vector.

54. An agent as claimed in claim 53 comprising a vector binding to VEGF receptors.

55. An agent as claimed in claim 53 comprising a vector binding to the complex between an angiogenic factor and its receptor.

56. An agent as claimed in claim 53 wherein the vector binds to an endoglin.

57. An agent as claimed in claim 53 wherein the vector binds to an integrin.

58. An agent as claimed in claim 57 wherein the vector is an RGD-peptide.

59. An agent as claimed in claim 57 wherein the vector is a non-peptide RGD analogue.

60. An agent as claimed in claim 57 wherein the vector is selected from the group consisting of vectors binding to one or more of the following angiogenesis targets: integrins β_1, β_3 and β_5, $\alpha_v\beta_3$, $\alpha_6\beta_1$, $\alpha_2\beta_1$, $\alpha_v\beta_5$, α_6 and α_5.

61. An agent as claimed in claim 60 wherein the vector binds to the integrin $\alpha_v\beta_3$.

62. An agent as claimed in claim 38 wherein the vector binds to thrombi, i.e. platelet or fibrin.

63. An agent as claimed in claim 38 comprising a vector which bindsto endothelin receptors.

64. An agent as claimed in claim 38 comprising a vector which binds to an E-selectin receptor.- -

REMARKS

Applicants have submitted the revised executed Declaration and the substitute specification as allowed in response to the Examiner's requirements which incorporated corrections to some of the formulas, added new drawings to the application and submitted corrections and additions to the sequence listing by amendment in the parent application. A copy of the sequence listing in computer readable form which corresponds to the paper copy has also been submitted herewith.

Applicants have amended the claims taking into consideration the prosecution in the parent application. The original claims 1-37 have been canceled from the application and new claims 38-64 have been added to more particularly define the invention.

Applicants believe that these claims are in full compliance with 35 U.S.C. §112 and are clearly patentable over the references of record in the parent applications.

The present application is a continuation application and the prior art cited in the parent applications should be taken into consideration in the present application. In accordance with MPEP §2001.06(b) no copies of the prior art in the parent applications are submitted herewith. The reference cited forms from the parent applications are submitted herewith for the convenience of the Examiner. In accordance with MPEP §609, a Form 1449 listing these references is also submitted herewith. Confirmation that the prior art cited in the parent applications has been considered in the next Official Action is most respectfully requested.

In view of the above amendments to the specification and claims an early and favorable action on the merits is now in order and is most respectfully requested.

Respectfully submitted,

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